REMARKS

Applicants have amended the specification to reference the prior filed applications from which the instant application claims benefit. Applicants respectfully contend that the requirements for submitting such an amendment under 37 C.F.R. §1.78(a)(2)(ii) and (a)(3) should be waived because the U.S. PTO has recognized the claim for benefit on both the Filing Receipt and on the cover page of the related U.S. Patent Application Publication (copies of which are attached). Applicants note that the Notice on Claiming the Benefit of Prior-Filed Applications from Deputy Commissioner Stephan Kunin dated February 24, 2003 specifically states that the requirements under 37 C.F.R. §1.78(a)(3)(ii) and (iii) will be waived if the "information concerning the claim was recognized by the Office as shown by its inclusion on the filing receipt."

Claims 1-53 are pending in the instant application. The Examiner has stated that restriction to one of the following inventions is required under 35 U.S.C. 121:

I. The compounds and composition according to Claim 1.
II. The compounds and composition according to Claim 10.
III. The method of treating according to Claim 29-53.

The Examiner has alleged that the inventions of Group I-III are separate and patentably distinct because there is no patentable co-action among them and a reference anticipating one member will not render another obvious. The Examiner has further alleged that a search of the three groups designated above would impose an undue burden upon the examiner, and restriction for examination purposes as indicated is proper. The Examiner advised Applicants that the reply to this requirement must include an election of a specifically disclosed species of the invention to be examined, even though the requirement is traversed, in order for the reply to be complete.

Applicants respectfully traverse the restriction. Applicants maintain that a search of the prior art which focuses on polymorphous salt forms of 4-[2-(5-cyano-thiazol-2-ylamino)-pyridin-4-ylmethyl]-piperazine-1-carboxylic acid methylamide would be comprehensive with respect to the instant invention yet would not require a serious burden on the Examiner. Applicants also respectfully request clarification as to which Group would cover independent claims 12, 14 and 19 (and their dependent claims). Applicants note that Section 803 of the MPEP provides:

> There are two criteria for a proper requirement for restriction between patentably distinct inventions:
> (1) The inventions must be independent or distinct as claimed;
> and
> (2) There must be a serious burden on the examiner if restriction is not required.

Additionally, MPEP 803 indicates that :

> If the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions.

Because there would be no serious burden on the Examiner in searching such closely related groups, Applicants respectfully contend that any restriction requirement would be improper. Additionally, Applicants respectfully note that research in the area of small molecule inhibitors of tyrosine kinase has taken place only in the last 20 years prior to the earliest priority date accorded the instant application. Applicants also note that the connection between tyrosine kinases, in particular KDR and macular degeneration, diabetic retinopathy and retinal ischemia has taken place only in the last 15 years. Applicants therefore respectfully contend that a search of the scientific and patent art in the twenty years prior to July 24, 2002 (the effective filing date of the instant application), for any disclosure of the use of the instant compound in the treatment of angiogenic associated diseases should be comprehensive with respect to the invention as originally claimed, yet clearly would not be an undue burden on the Examiner in light of the extensive electronic searching tools now available to the Examiner.

Applicants expressly note that Applicants are not arguing that the group elected by Applicants is not patentably distinct, but rather, contend that the Examiner should examine all of the groups of the instant invention since there would be no serious burden on the Examiner. For the reasons noted above, Applicants respectfully contend that the restriction requirement is improper and request that restriction be withdrawn.

However, to facilitate the Examiner's search under 37 C.F.R. 1.21 and to expedite prosecution of this application, Applicants elect Group I, which is directed to a polymorphous

form of a hydrochloride salt of 4-[2-(5-cyano-thiazol-2-ylamino)-pyridin-4-ylmethyl]-piperazine-1-carboxylic acid methylamide.

Applicants respectfully contend that Claims 1-53 as filed are allowable and an early Notice of Allowance is earnestly solicited. If a telephonic communication with Applicant's representative will aid in the advancement of the prosecution of this application, please telephone the representative indicated below.

Respectfully submitted,

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(54) **SALT FORMS WITH TYROSINE KINASE ACTIVITY**

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(57) **ABSTRACT**

The present invention relates to salt forms of 4-[2-(5-cyano-thiazol-2-ylamino)-pyridin-4-ylmethyl]-piperazine-1-carboxylic acid methylamide which inhibit, regulate and/or modulate tyrosine kinase signal transduction, compositions which contain these compounds, and methods of using them to treat tyrosine kinase-dependent diseases and conditions, such as angio-genesis, cancer, tumor growth, atherosclerosis, age related macular degeneration, diabetic retinopathy, retinal ischemia, macular edema, inflammatory diseases, and the like in mammals.

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Title

Salt forms with tyrosine kinase activity